AMENDMENTS TO THE SPECIFICATION

Page 71, amend the paragraph after the paragraph beginning "Fig. 2" as follows:

Fig. 2b. depicts a ~~methodolgy~~methodology for optimization;

Please delete the entire eighth paragraph on page 71.

On page 71, paragraphs nine through 12:

Figs. ~~8A and 8B~~7A and 7B are graphical illustrations of the output of the model of Fig. 3;

Figs. ~~9A and 9B~~8A and 8B are graphical illustrations of experimental data as compared to the output shown in Figs. ~~8A and 8B~~7A and 7B;

Fig. ~~10~~9 is a schematic illustration of a biological model, in accordance with a further embodiment of the present invention;

Fig. ~~11~~10 is a graphical illustration of results of the simulation of the model shown in Fig. ~~10~~9;

On page 72, paragraphs one through three:

Figs. ~~12A and 12B~~11A and 11B are graphical illustrations of the effects of two doses of G-CSF on the Neutrophil line, according to the model of Fig. ~~10~~9;

Fig. ~~13~~12 is a schematic illustration of a biological model, in accordance with a further embodiment of the present invention;

Figs. ~~14 and 15~~13 and 14 show a comparison of Neutrophil production according to the described model and experimental data in the literature.

On page 85, amend the paragraph after the paragraph beginning "Fig. 2" as follows:

The cells of MK16 compartment 60 are megakaryocytes of 16N-ploidy class that release platelets (Plt) at a constant uniform rate (γ_{MK16}) until they exhaust their capacity (C_{MK16}, for example), and then are disintegrated. For background details, see, Harker LA, Finch CA: Thrombokinetics in man. *J Clin Invest.* 1969; Vol.48; pp. 963-974; and Eller J, Gyori I *et al*: ~~Modelling~~ Modeling Thrombopoiesis regulation – I: model description and simulation results. *Comput Math Applic.* 1987; Vol. 14 (9-12); pp. 841-848.

On page 110, first full paragraph:

~~Reference is now made to Fig. 7, which is a graphical representation of the chart of Fig. 6, and is the most useful model output.~~ The implementation of the described model results in a computer simulator that describes the changes that occur in the human Thrombopoietic system (platelet counts, bone marrow precursor numbers, and TPO concentration) over a time span that may last several years. The resolution of the simulator output is one hour.

In the paragraph bridging pages 114 and 115:

Reference is now made to Figs. ~~8A, 8B, 9A and 9B~~7A, 7B, 8A and 8B, which show a comparison between experimentally obtained data and the simulated model. Experimentally obtained *in vivo* platelet counts following TPO administration are shown in Fig. ~~8A~~7A and chemotherapy without TPO is shown in Fig. ~~9A~~8A. Figs. ~~8B and 9B~~7B and 8B show simulations of the same. By using a TPO schedule designed by the described model, one can obtain platelet profiles that are similar to those obtained clinically (Fig. ~~8B~~7B) or even more effective (Fig.

~~9B~~8B). In this case, these results are achieved by administering a pre-calculated TPO protocol whose total dose amounts to 25% of the original total dose.

On page 115, after the first unfinished paragraph, insert the following paragraphs:

Fig 8A and B show TPO given to healthy donors: Results of TPO clinical trials from recent research on healthy platelet donors, as compared to our computer simulation results. (A) Comparison of experimental data from the literature (dots) and our model simulation (solid line). In both cases, TPO was given as a single IV dose of 1.2 μg/kg on day 0. (B) Comparison of the same experimental data (dots) and our proposed TPO administration protocol; the total dose in the simulated protocol was 0.3 μg/kg (solid line).

Figs. 9A and B show TPO with chemotherapy: (A) Results of clinical trials from recent research on thrombocytopenia induced in patients receiving single carboplatin chemotherapy on day 0 (dots connected by line), as compared to our model simulation of these results (continuous solid line). (B) The same experimental data (dots connected by line) compared to simulations of the same chemotherapy protocol, with addition of "conventional" TPO as a single IV dose of 1.2 μg/kg on day 0 (continuous solid line) and simulations of the same chemotherapy protocol combined with our proposed TPO protocol, using a total of 0.3 μg/kg TPO (dotted line).

On page 126, second full paragraph:

Reference is now made to Figs. ~~14 and 25~~13 and 14 which show a comparison of Neutrophil production according to the described model and experimental data in the literature. Increased Neutrophil production is in accordance with the Neutrophil counts reported by Price et

al. In addition, these increases are in accordance with Price's data about Neutrophil bone marrow pool sizes.

On page 130, second full paragraph:

Reference is now made to Fig. ~~11~~10, which is a graphical illustration of a simulation of the model. Though no empirical data is available on this point, simulations of the model predict that the number of cells in the post-mitotic compartment decreases substantially during the first two days of G-CSF administration, and then replenishes, so that on the sixth day the counts return almost to their normal levels. This replenishment lags behind that of Price et al report by a few hours. A **testable hypothesis** can thus be formulated, i.e., whether using the same G-CSF protocol Price et al used, there is indeed a nadir on day 3 of the treatment.

On page 132, first full paragraph:

Reference is now made to Figs. ~~12A and 12B~~11A and 11B, which are graphical illustrations of the effects of G-CSF at the two doses. The effects as a function of G-CSF level are connected piece-wise linearly. This way, the Neutrophil levels observed clinically under both the 300 and the 30-μgram protocols are obtained.

On page 140, second full paragraph:

Reference is now made to Fig. ~~13~~12, which is a schematic illustration of the tumor cell cycle layer. The whole cycle is divided into 4 compartments, or stages (G_1, S, G_2 and M). Each compartment is divided into equal subcompartments, where i^{th} subcompartment in each stage represents cells of age i in the particular stage (i.e. they have spent i time-steps in this stage). The

quiescent stage is denoted G_0. The cell cycle follows a direction as shown by arrows (#). Thus, cells enter each stage starting with the first subcompartment, denoted G_1.